Prognostic Significance of Electrocardiographic Voltages and Their Serial Changes in Elderly With Systolic Hypertension

Robert H. Fagard, Jan A. Staessen, Lutgarde Thijs, Hilde Celis, Willem H. Birkenhager, Christopher J. Bulpitt, Peter W. de Leeuw, Gastone Leonetti, Cinzia Sarti, Jaakko Tuomilehto, John Webster, Yair Yodfat, for the Systolic Hypertension in Europe (Syst-Eur) Trial Investigators

Abstract—The aim of the present study was to assess the prognostic value of ECG voltages at baseline and their serial changes during follow-up in a large prospective study with standardized follow-up and strictly defined end points. Patients who were 60 years old or older, with systolic blood pressure of 160 to 219 mm Hg and diastolic pressure <95 mm Hg, were randomized into the double-blind placebo-controlled Systolic Hypertension in Europe trial. Active treatment consisted of nitrendipine, which could be combined with or replaced by enalapril, hydrochlorothiazide, or both. At the end of the double-blind part of the trial (median follow-up, 2.0 years), follow-up was extended and all patients received active study drugs (median total follow-up, 6.1 years). Electrocardiography was performed at baseline and yearly thereafter. Electrocardiographic left ventricular mass was prospectively defined as the sum of 3 voltages (RaVL + SV1 + RV5), which averaged 3.1 ± 1.0 mV. The adjusted relative hazard rate, associated with a 1-mV higher sum at baseline, amounted to 1.10 and 1.15 for all-cause and cardiovascular mortality and to 1.21 and 1.18 for strokes and cardiac events, respectively (P ≤ 0.01 for all). A 1-mV decrease in electrocardiographic voltages during follow-up independently predicted a lower incidence of cardiac events (relative hazard rate: 0.86; P ≤ 0.05), but not of stroke or mortality. In conclusion, electrocardiographic voltages at baseline and their serial changes during follow-up predict subsequent events in older patients with systolic hypertension. (Hypertension. 2004;44:459-464.)

Key Words: antihypertensive therapy ■ elderly ■ electrocardiography ■ hypertension, essential ■ hypertrophy, cardiac ■ prognosis

There is convincing evidence that electrocardiographic (ECG) and echocardiographic (ECHO) left ventricular hypertrophy (LVH) are associated with increased cardiovascular morbidity and mortality,1–7 but the independent prognostic implications of LVH regression remain a matter of debate.8–14 The possible benefit of LVH regression has been extended and all patients received active study drugs (median total follow-up, 6.1 years). Electrocardiography was performed at baseline and yearly thereafter. Electrocardiographic left ventricular mass was prospectively defined as the sum of 3 voltages (RaVL + SV1 + RV5), which averaged 3.1 ± 1.0 mV. The adjusted relative hazard rate, associated with a 1-mV higher sum at baseline, amounted to 1.10 and 1.15 for all-cause and cardiovascular mortality and to 1.21 and 1.18 for strokes and cardiac events, respectively (P ≤ 0.01 for all). A 1-mV decrease in electrocardiographic voltages during follow-up independently predicted a lower incidence of cardiac events (relative hazard rate: 0.86; P ≤ 0.05), but not of stroke or mortality. In conclusion, electrocardiographic voltages at baseline and their serial changes during follow-up predict subsequent events in older patients with systolic hypertension. (Hypertension. 2004;44:459-464.)

Methods

Trial Design

Patients with systolic hypertension, aged 60 years or older, were randomized into the double-blind placebo-controlled Syst-Eur trial, in which active treatment consisted of nitrendipine, with the possible addition of enalapril and/or hydrochlorothiazide (phase 1).15 When phase 1 of the trial was stopped in February 1997, after a median follow-up of 2.0 years (range, 1 month to 8.1 years),15 all patients...
received active study treatment during extended follow-up until December 2001 (phase 2). The placebo group in phase 1 of the trial is termed “control group” in the current report and the actively treated group “active treatment group.” The protocol was approved by the Ethics Committees of the University of Leuven and participating centers; patients gave informed consent.

At each follow-up visit, BP was the average of 2 BP measurements in the sitting position, by use of standard sphygmomanometry. Baseline BP was the average of 2 BP at each of 3 visits. A standard 12-lead ECG was performed at baseline and yearly thereafter. As predefined in the protocol, investigators at the coordinating office measured the voltages of SV1, RaVL, and RV5 (mV). ECG LVM was defined as the sum of RaVL + SV1 + RV5 and ECG-LVH as RaVL + SV1 + RV5 > 4.7 mV.

All events that occurred during follow-up were corroborated by the Syst-Eur End Point Committee. Outcome variables were: (1) Fatal and nonfatal strokes. Stroke was defined as a neurological deficit with symptoms continuing for >24 hours or leading to death with no apparent cause other than vascular. (2) Fatal and nonfatal coronary heart disease, comprising acute myocardial infarction and sudden death. Myocardial infarction was defined as 2 of the following 3 disorders: typical chest pain, electrocardiographic changes, and increased cardiac enzymes. Sudden death included any death of unknown origin occurring immediately or within 24 hours of the onset of acute symptoms, as well as unattended death for which no likely cause could be established by necropsy or medical history. Angina pectoris and arrhythmias were not included, unless fatal. (3) Fatal and nonfatal heart failure, irrespective of hospitalization. The diagnosis required the presence of the following 3 disorders or symptoms: (a) dyspnea; (b) clinical signs (such as ankle edema or pulmonary crepitations); and (c) the necessity of treatment with diuretics, vasodilators, or antihypertensive drugs. (4) All cardiac events comprise coronary heart disease and heart failure as defined. (5) All cardiovascular events comprise all strokes and all cardiac events as defined. (6) Cardiovascular mortality, including all fatal cardiovascular events. (7) All-cause mortality.

### Statistical Analysis

Database management and statistical analysis were performed using SAS software, version 6.12 (SAS Institute Inc). Data are reported as mean±SD or as proportions. Comparisons between groups were performed by Student unpaired t tests or by χ² tests. The prognostic significance of baseline ECG voltages and ECG LVH was assessed by Cox regression analysis on patients in whom a baseline ECG was available, with exclusion of patients with previous myocardial infarction or concomitant systolic BP changes. In the combined analysis of the 2 study groups, we also adjusted for age, gender, body mass index, smoking, systolic BP, pulse rate, diabetes, and previous antihypertensive treatment and cardiovascular complications at baseline. In the analysis of ECG changes during follow-up, we also adjusted for baseline ECG voltages and concomitant systolic BP changes. In the combined analysis of the 2 study groups, we also adjusted for study group. In patients with >1 cardiovascular event, the first relevant event was considered in each of the analyses. Relative hazard rates reflect the risk associated with a 1-mV higher value of RaVL + SV1 + RV5 or the presence of LVH at baseline, or a 1-mV decrease in ECG voltages during follow-up. A 2-tailed P ≤ 0.05 was considered significant.

### Results

#### Patient Characteristics at Baseline

Among the 4695 patients randomized in the Syst-Eur trial, 165 patients had a previous myocardial infarction, 6 a left bundle branch block, 10 an artificial pacemaker, and 7 had missing voltages or calibration signal on the ECG, leaving 4507 patients for the analysis on baseline ECG. Of these 4507 patients, 348 were excluded from the analysis on the follow-up ECG, because of premature death (n = 52), myocardial infarction (n = 23) or pacemaker implantation (n = 2), interruption of regular follow-up (n = 152), missing/incomplete ECG (n = 118), or newly developed left bundle branch block (n = 1). The characteristics of the 4507 and 4159 patients are given in Table 1 and were not significantly different between the active treatment group and the control group.

#### Prognostic Significance of Baseline ECG Voltages

Median follow-up of the 4507 patients after randomization was 6.1 years (range, 0.1 to 13 years); total follow-up time was 28 743 patient-years. Table 2 summarizes the number of events and the relative hazard rates reflecting the risk associated with a 1-mV greater sum of RaVL + SV1 + RV5. In the combined analysis of the 2 treatment groups, ECG voltages significantly and independently predicted total and cardiovascular mortality, all strokes, all cardiac events, coronary heart disease, heart failure, and aggregate fatal and nonfatal cardiovascular events (P ≤ 0.01). The relative hazard rate for sudden death was significant before 1.24; 95% confidence interval [CI], 1.05 to 1.45; P ≤ 0.05)
TABLE 2. Relative Hazard Rates Relating Baseline ECG Voltages (RaVL + SV1 + RV5) to the Incidence of Events

<table>
<thead>
<tr>
<th>Active treatment group</th>
<th>Mortality</th>
<th>Fatal and Nonfatal Cardiovascular Events</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>Control group</td>
<td>368</td>
<td>192</td>
</tr>
<tr>
<td>Crude</td>
<td>1.16#</td>
<td>(1.06–1.28)</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>1.10#</td>
<td>(1.00–1.21)</td>
</tr>
<tr>
<td>Both groups</td>
<td>689</td>
<td>350†</td>
</tr>
<tr>
<td>Crude</td>
<td>1.17**</td>
<td>(1.09–1.25)</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>1.10†</td>
<td>(1.02–1.18)</td>
</tr>
</tbody>
</table>

Relative hazard rates (95% confidence interval) reflect the risk associated with a 1-mV higher value of RaVL + SV1 + RV5.

N indicates number of events; CHD, coronary heart disease; HF, heart failure; MI, myocardial infarction; SD, sudden death.

*Adjusted relative hazard rates account for age, gender, body mass index, smoking, systolic blood pressure and pulse rate, diabetes, previous antihypertensive treatment, and cardiovascular complications at baseline, and also for study group for the combined analysis of both groups.

†N of (first) cause-specific events in each category: †89 strokes; 54 MI; 122 SD; 49 HF; 7 aortic aneurysm; 9 pulmonary embolism; 20 others. ‡219 strokes; 163 MI; 103 SD; 176 HF. §172 MI; 108 SD; 182 HF. ¶182 MI; 117 SD.

but not after adjustment (1.16; 95% CI, 0.98 to 1.37). The adjusted relative risk of ECG LVH at baseline was 1.51 (95% CI, 1.20 to 1.91) and 1.72 (95% CI, 1.26 to 2.35) for, respectively, total and cardiovascular mortality (P ≤ 0.001), 1.68 (95% CI, 1.33 to 2.13) (P ≤ 0.001) for all cardiovascular events, and, respectively, 1.72 (95% CI, 1.17 to 2.52) (P ≤ 0.01) and 1.72 (95% CI, 1.30 to 2.28) (P ≤ 0.001) for strokes and cardiac events.

**Prognostic Significance of Changes in ECG Voltages During Follow-Up**

A total of 22,412 follow-up ECG were recorded in the 4159 patients during the trial. Median follow-up after the first follow-up ECG was 5.1 years (range, 0.003 to 11.8 years) in the active treatment group and 5.1 years (range, 0.003 to 12.0 years) in the control group; total follow-up times were, respectively, 11,863 and 11,316 patient-years. Placebo treatment was gradually replaced by active therapy in the control group as more patients entered phase 2 of the trial. The Figure illustrates the changes in ECG voltages and in BP during follow-up. In multiple regression analysis, after adjustment for baseline ECG voltages, reductions in ECG voltages were more pronounced in the presence of greater decreases in systolic BP (P < 0.05).

Table 3 summarizes the results on the prognostic significance of changes in ECG voltages during follow-up when entered as a time-dependent variable. In both groups taken together, changes in ECG voltages predicted cardiac events independently of baseline ECG voltages and other covariates, including changes in systolic BP. A 1-mV decrease in ECG voltages was associated with a 14% reduction in all cardiac events and a 16% reduction in coronary heart disease risk (P ≤ 0.05). ECG changes during follow-up did not predict total mortality, cardiovascular mortality, sudden death or the incidence of stroke. In the analysis in which the last available ECG was used, the risk reduction in cardiac events and coronary heart disease amounted to, respectively, 17% and 21% (P ≤ 0.01) (Table 4).

**Discussion**

The current study extends the generally accepted prognostic significance of LVH/LVM to elderly patients with systolic hypertension, and gives strength to the suggestion that treatment-induced reductions in LVH/LVM have independent prognostic power. In the separate analysis of the 2 treatment groups, the latter finding was significant in the group that received active treatment throughout the trial, but not in the control group in which subjects received placebo during phase 1 of the trial and active therapy during phase 2, after having been in phase 1 for variable periods of time.

There is little doubt that ECHO LVH and ECG LVH are associated with increased incidence of cardiovascular events. ECG studies have used a variety of criteria to define LVH, usually including voltage measurements, but it is well known that the ECG has relatively low sensitivity for the detection of LVH. Furthermore, this approach does not consider the full quantitative range of ECG voltages. In the current study, we measured voltages in 3 leads reflecting potentials from the left ventricle. The sum of RaVL + SV1 + RV5 predicted all-cause and cardiovascular mortality, stroke, cardiac events, and all cardiovascular events combined. A 1-mV higher value was associated with a 19% greater risk of a cardiovascular event, independent of important confounders including age, gender, and BP.

Whereas the prognostic significance of LVH is well accepted, there is less certainty on the independent prog-
nostic power of regression of LVH or reductions in LVM. Several studies have used echocardiography to examine associations between categorical changes in LVH and outcome in patients with hypertension.9–11,13 All but one study 11 reported significant relationships between such changes and various aggregates of cardiovascular events. These echocardiographic studies were usually retrospective, with small numbers of participants or few events. Two studies have been published on the prognostic implications of regression of ECG LVH. Levy et al8 included 524 men and women from the Framingham Heart Study, with ECG evidence of LVH, irrespective of BP. Subjects with a serial decline in ECG voltage quartile (RaVL/SV1/RV5; mV) and in systolic and diastolic blood pressure (mm Hg) in the control group (C; ○) and in the active treatment group (A; ●) during 8 years of follow-up *P<0.05; **P<0.01; +P<0.001 for the difference between the 2 groups.

Changes from baseline in ECG voltages (RaVL/SV1/RV5; mV) and in systolic and diastolic blood pressure (mm Hg) in the control group (C; ○) and in the active treatment group (A; ●) during 8 years of follow-up *P<0.05; **P<0.01; +P<0.001 for the difference between the 2 groups.

Strengths of the current study are the prospective design, the large sample size, the large number of events allowing cause-specific analyses, the blinded evaluation of the events by an End Point Committee, and the yearly recorded ECG. However, several limitations have to be considered. Because of the 198 centers involved in Eastern and Western Europe and the older study population, echocardiography was not included in the protocol of the trial. The quantitative ECG analysis was limited to the simple measurement of 3 predefined voltages, reflecting the left ventricle, as in the EWPHE trial conducted by the same investigators.23,24 In the current study and in previous reports,17,24 the sum of RaVL/SV1/RV5 was significantly related to systolic BP. In a post hoc analysis of 74 patients from a previous study of our group,25 in which ECHO LVH was measured in well-standardized conditions, the correlation coefficient of RaVL/SV1/RV5 with ECHO LVM was 0.43, and amounted to 0.46 when LVM was indexed for body surface area (P<0.001). Finally, the analysis on the prognostic significance of the follow-up ECG was limited to patients who had at least 1 ECG after randomization.

Perspectives
The current study supports the suggestion that regression of LVH/LVM can be considered a surrogate end point for morbid events in hypertension treatment trials.26 The relationship of LVH/LVM and of the changes of LVH/
TABLE 3. Relative Hazard Rates Relating Serial Changes in ECG Voltages (RaVL+SV1+RV5) During follow-up to the Incidence of Events

<table>
<thead>
<tr>
<th></th>
<th>Mortality</th>
<th>Fatal and Nonfatal Cardiovascular Events</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>Active treatment group</td>
<td>268</td>
<td>130</td>
</tr>
<tr>
<td>Baseline ECG*</td>
<td>1.05 (0.92–1.20)</td>
<td>1.18 (0.97–1.42)</td>
</tr>
<tr>
<td>Delta ECG*</td>
<td>1.00 (0.85–1.16)</td>
<td>0.90 (0.73–1.12)</td>
</tr>
</tbody>
</table>

Control group

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>297</th>
<th>147</th>
<th>274</th>
<th>112</th>
<th>186</th>
<th>121</th>
<th>83</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline ECG*</td>
<td>1.14† (1.01–1.28)</td>
<td>1.15 (0.97–1.36)</td>
<td>1.18$ (1.04–1.34)</td>
<td>1.13 (0.92–1.38)</td>
<td>1.21† (1.04–1.40)</td>
<td>1.24† (1.03–1.49)</td>
<td>1.26† (1.01–1.58)</td>
<td></td>
</tr>
<tr>
<td>Delta ECG*</td>
<td>0.90 (0.78–1.05)</td>
<td>0.95 (0.76–1.17)</td>
<td>0.97 (0.82–1.14)</td>
<td>0.95 (0.74–1.22)</td>
<td>0.93 (0.77–1.13)</td>
<td>0.90 (0.71–1.13)</td>
<td>0.95 (0.71–1.26)</td>
<td></td>
</tr>
</tbody>
</table>

Both groups

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>565</th>
<th>277</th>
<th>538</th>
<th>195</th>
<th>377</th>
<th>237</th>
<th>177</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline ECG*</td>
<td>1.10† (1.01–1.20)</td>
<td>1.15† (1.02–1.31)</td>
<td>1.22$ (1.11–1.33)</td>
<td>1.20† (1.03–1.39)</td>
<td>1.24$ (1.11–1.38)</td>
<td>1.23$ (1.08–1.41)</td>
<td>1.31$ (1.12–1.53)</td>
<td></td>
</tr>
<tr>
<td>Delta ECG*</td>
<td>0.95 (0.85–1.05)</td>
<td>0.93 (0.80–1.09)</td>
<td>0.90 (0.81–1.01)</td>
<td>0.97 (0.81–1.17)</td>
<td>0.86$ (0.76–0.98)</td>
<td>0.84$ (0.71–0.99)</td>
<td>0.91 (0.76–1.10)</td>
<td></td>
</tr>
</tbody>
</table>

Changes in ECG voltages are entered as time-dependent covariates in the Cox regression models. Relative hazard rates (95% confidence interval) reflect the risk associated with a 1-mV higher sum of SV1+RV5+RaVL for baseline ECG and the risk associated with a 1-mV decrease in SV1+RV5+RaVL for delta ECG.

N indicates number of events; CHD, coronary heart disease; HF, heart failure; MI, myocardial infarction; SD, sudden death.

†P<0.05; ‡P<0.01; §P<0.001.

LVM with subsequent morbid events appears to be consistent. In the current study, we found that ECG voltages can be used as a quantitative variable, which is an advantage over categorical analyses, in which patients may remain in the same LVH category despite a relevant change in ECG LVH. Furthermore, electrocardiography is possible in all patients and is less costly and time-consuming than echocardiography. Whereas there is currently no strong evidence from directly comparative studies, that first-line agents differ in their effects on LVH/LVM, except perhaps for angiotensin II antagonists, quantitative electrocardiography can probably contribute to the assessment of the effects of newer drugs on LVH/LVM in large study groups.

TABLE 4. Relative Hazard Rates Relating Changes in ECG Voltages (RaVL+SV1+RV5) From Baseline to the Last Available ECG or to the Last ECG Before the Event in Case of an Event to the Incidence of Events

<table>
<thead>
<tr>
<th></th>
<th>Mortality</th>
<th>Fatal and Nonfatal Cardiovascular Events</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>Active treatment group</td>
<td>268</td>
<td>130</td>
</tr>
<tr>
<td>Baseline ECG*</td>
<td>1.05 (0.92–1.20)</td>
<td>1.17 (0.97–1.41)</td>
</tr>
<tr>
<td>Delta ECG*</td>
<td>0.96 (0.84–1.11)</td>
<td>0.88 (0.73–1.08)</td>
</tr>
</tbody>
</table>

Control group

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>297</th>
<th>147</th>
<th>274</th>
<th>112</th>
<th>186</th>
<th>121</th>
<th>83</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline ECG*</td>
<td>1.14† (1.02–1.29)</td>
<td>1.17 (0.99–1.39)</td>
<td>1.20$ (1.05–1.36)</td>
<td>1.15 (0.94–1.40)</td>
<td>1.22$ (1.05–1.43)</td>
<td>1.27$ (1.05–1.53)</td>
<td>1.28$ (1.02–1.61)</td>
<td></td>
</tr>
<tr>
<td>Delta ECG*</td>
<td>0.88 (0.76–1.01)</td>
<td>0.86 (0.71–1.06)</td>
<td>0.90 (0.78–1.04)</td>
<td>0.89 (0.71–1.14)</td>
<td>0.86 (0.72–1.03)</td>
<td>0.82 (0.66–1.02)</td>
<td>0.88 (0.68–1.15)</td>
<td></td>
</tr>
</tbody>
</table>

Both groups

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>565</th>
<th>277</th>
<th>538</th>
<th>195</th>
<th>377</th>
<th>237</th>
<th>177</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline ECG*</td>
<td>1.10† (1.01–1.21)</td>
<td>1.16† (1.02–1.31)</td>
<td>1.23$ (1.12–1.34)</td>
<td>1.21† (1.04–1.40)</td>
<td>1.25$ (1.12–1.39)</td>
<td>1.25$ (1.10–1.43)</td>
<td>1.31$ (1.12–1.53)</td>
<td></td>
</tr>
<tr>
<td>Delta ECG*</td>
<td>0.92 (0.83–1.02)</td>
<td>0.88 (0.77–1.02)</td>
<td>0.86$ (0.78–0.95)</td>
<td>0.92 (0.77–1.09)</td>
<td>0.83$ (0.74–0.94)</td>
<td>0.79$ (0.68–0.92)</td>
<td>0.89 (0.75–1.06)</td>
<td></td>
</tr>
</tbody>
</table>

Relative hazard rates (95% confidence interval) reflect the risk associated with a 1-mV higher sum of SV1+RV5+RaVL for baseline ECG and the risk associated with a 1-mV decrease of SV1+RV5+RaVL for delta ECG.

The relative hazard rates for baseline ECG voltages and changes in ECG voltages (delta ECG) are mutually adjusted and also account for age, gender, body mass index, smoking and pulse rate, diabetes, previous antihypertensive treatment and cardiovascular complications at baseline, baseline systolic BP and changes in systolic BP during follow-up, and also for study group in the combined analysis of both groups.
Acknowledgments

The Syst-Eur Trial was a concerted action of the BIOMED Research Program sponsored by the European Union. The trial was sponsored by Bayer AG (Wuppertal, Germany). The National Fund for Scientific Research (Brussels, Belgium) provided additional support. Study medication was donated by Bayer AG, Merck Sharp, and Dohme Inc (West Point, Pa). The trial was performed in consultation with the World Health Organization, the International Society of Hypertension, the European Society of Hypertension, and the World Hypertension League. A list of the original Syst-Eur Trial participants is available in Staessen JA, Fagard R, Thijss L, Arabidzge GG, Birkenhager WH, Bulppit CJ, de Leeuw PW, Dollery CT, Fletcher AE, Forette F, Leonetti G, Nachev C, O’Brien ET, Rosenfeld J, Rodicio JL, Tuomilehto J, Zanchetti A. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. *Lancet*. 1997;350:757–764 and the updated list is available at www.kuleuven.ac.be/hypertension/systeur/index.htm. The authors have no conflicts of interest. The authors gratefully acknowledge the secretarial assistance of Nicole Ausseleos.

References


Prognostic Significance of Electrocardiographic Voltages and Their Serial Changes in Elderly With Systolic Hypertension

Robert H. Fagard, Jan A. Staessen, Lutgarde Thijs, Hilde Celis, Willem H. Birkenhäuser, Christopher J. Bulpitt, Peter W. de Leeuw, Gastone Leonetti, Cinzia Sarti, Jaakko Tuomilehto, John Webster and Yair Yodfat

for the Systolic Hypertension in Europe (Syst-Eur) Trial Investigators

Hypertension. 2004;44:459-464; originally published online August 23, 2004;
doi: 10.1161/01.HYP.0000142169.17298.54

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/44/4/459

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/